

CLAIMS

That which is claimed is:

1. A method for resurfacing a rabbit antibody, said method comprising:
5 (a) identifying a surface-exposed amino acid of a framework region of a parent rabbit antibody that differs from an amino acid at a corresponding position of a non-rabbit antibody by comparing the amino acid sequence of said framework region of said parent rabbit antibody to the amino acid sequence of said framework region of said non-rabbit antibody; and
(b) substituting said identified amino acid with an amino acid at said corresponding
10 position of a non-rabbit antibody,
to resurface said rabbit antibody.
2. The method of claim 1, further comprising identifying amino acids of said framework region of a parent antibody that are proximal to a CDR and substituting only those amino acids
15 that are not proximal to said CDR.
3. The method of claim 1, further comprising identifying amino acids in a D-E loop region of said parent antibody and substituting only those amino acids that are not in said D-E loop.
- 20 4. The method of claim 1, wherein said identifying step involves molecular modeling of said parent rabbit antibody or said non-rabbit antibody to identify said surface-exposed amino acids.
5. The method according to Claim 1, wherein said identifying step (a) comprises identifying a plurality of amino acids and step (b) comprises substituting said plurality of amino acids.
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6. The method according to Claim 5, wherein said plurality of amino acids is at least two discontinuous amino acid.

7. The method according to Claim 1, wherein said method is a method of humanizing a rabbit monoclonal antibody.

8. The method according to Claim 1, wherein a modified rabbit antibody comprising a framework region having said substituted amino acid is less immunogenic in a non-rabbit host than said rabbit parent antibody.

9. The method according to Claim 1, wherein said identifying step (a) comprises identifying amino acids that may be inserted into or deleted from said framework region of said parent rabbit antibody and said substituting step (b) comprises inserting into or deleting said amino acids from said nucleic acid sequence.

10. The method according to Claim 1, wherein said rabbit antibody from a rabbit of known V_H allotype.

11. The nucleic acid according to Claim 10, wherein said rabbit antibody is from a rabbit that is homozygous for a V_H allotype.

12. The nucleic acid according to Claim 19, wherein said rabbit is homozygous for an allotype chosen from V_{H1} -a1, V_{H1} -a2 and V_{H1} -a3.

13. The method according to Claim 1, wherein said resurfaced antibody has a binding affinity of $10^8 M^{-1}$ or greater for a specific antigen.

14. A monoclonal antibody that has been resurfaced by the method set forth in claim 1.

15. A nucleic acid encoding the monoclonal antibody of claim 14.

16. A vector comprising the nucleic acid of Claim 15.

17. A host cell comprising the vector according to Claim 16.

18. A method of producing a modified rabbit antibody that is less immunogenic in a non-rabbit host as compared to its parent rabbit antibody, said method comprising:

- 5 incubating the host cell of Claim 17 under conditions sufficient to produce said antibody;
and
 harvesting said antibody.

19. A computer-readable medium encoding instructions to direct a machine to perform the
10 method of Claim 1.

20. A kit for use in a computer, said kit comprising:

- (a) a computer-readable medium according to Claim 19; and
(b) instructions for operating said computer according to said programming.

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